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Growth and characterisation of Atenolol - An antihypertensive drug

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Abstract

In pharmaceutical field, the search for compounds that have suitable properties to be used is nowadays a big challenge. Atenolol, one of the most widely used â-Blockers, clinically used as a reference drug in randomized controlled trials of hypertension. Single crystals of Atenolol have been grown successfully by slow evaporation of an ethanol/water solution. The modes of vibration of different groups present in the crystals are identified by FT-IR technique. The range and percentage of optical transmission as well as absorption are ascertained by recording UV-Vis-NIR spectrum. To understand the thermal properties, TGA and DTA were carried out. The surface morphology of the crystal were analysed by Scanning Electron Microscope. Grown crystals have been characterized using Powder X-ray diffraction and energy dispersive X-ray spectroscopy (EDAX).

Keywords: crystal growth, EDAX, infrared spectroscopy, thermo gravimetric analysis.

INTRODUCTION

Since bioavailability and properties related to formulation depend on the crystalline structure, their knowledge are essential in pharmaceutical technology (Grant,1999; Bym et al., 1999;Bemstein, 2002). A factor often associated with the difficulties in the crystallization of organic compounds is the conformational diversity in solution. Molecules of large size exhibit numerous conformational possibilities giving rise to crystal or amorphous solid materials. (Hilfiker, 2006; Bemstein, 2002) . This article deals with the growth of Atenolol, RS 2-{4-(2-hydroxy-3(propane-2ylamino) propoxy) phenyl} acetamide, a compound widely prescribed in medicine as a cardio selective â1-adrenergic blocker. It does not have membrane stabilizing and intrinsic sympathomimetic activities. Besides being one of the most widely used â blockers clinically, it has often been used as a reference drug in randomized controlled trials of hypertension. In this paper, the results of our work on the growth of Atenolol crystal along with the characterisation by Powder x-ray diffraction, Fourier Transform Infrared Transmission (FTIR) spectrum, UV-Vis-NIR analysis, Thermal analysis ,Scanning Electron Microscope (SEM) with EDAX analysis have been reported..

MATERIALS AND METHODS

Growth of Atenolol crystals

Atenolol crystals were grown by slow evaporation of the solvent in ethanol/water. A 0.1M solution of Atenolol in 20:80 volume per cent ethanol/water was evaporated at 25°C.The crystals were obtained within 15 days and were dried and kept in desiccators.

RESULTS AND DISCUSSION

FTIR Spectral Study

Infrared spectrometry involves examination of the twisting, bending, rotating and vibrational modes of atoms in a molecule. Upon interaction with infrared radiation portions of the incident radiation are absorbed at specific wavelengths. The occurrence of multiplicity of vibrations simultaneously produces a highly complex absorption spectrum that is uniquely a characteristic of the functional groups that make up the molecule and of the overall configuration of the molecule as well as FTIR spectrum of Atenolol crystal was carried out in the range 400-4000cm^{-1}The functional groups present in Atenolol were identified with the help of data.The spectrum obtained is shown in the Figure 1. The peak in the higher energy region between 3355.69cm^{-1},3172.68cm^{-1},2963.80cm^{-1},2064.70cm^{-1} were due to OH stretching ,NH stretching,CH_2 Stretching,CH stretching of alkyl group respectively. The weak peak at 1639.75cm^{-1} was due to C=O stretching frequency .The peaks at 1333.34cm^{-1},1241.44cm^{-1} were attributed to –OH bending and –C-O-C-stretching frequencies respectively. The in-plane C-H bending and out-of plane C-H bending are observed at 1037.45cm^{-1} and 707.58 cm^{-1} respectively. The peak at 802.5cm^{-1} shows the presence of p-dissubstituted

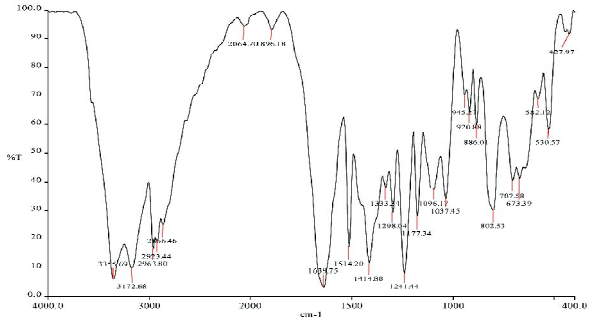

Fig.1 FTIR spectrum of grown crystal

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UV-VIS-NIR Spectral Analysis

Single crystals are mainly used in optical applications, optical transmission range and the transparency. UV-cut off is also important. The UV-VIS-NIR spectral transmittance was studied. The recorded spectrum is shown in the Figure 2. The crystal has sufficient transmission in the entire visible and IR region. The UV-cut off wavelength is around 224nm. And also it shows the crystal has a transmission of 94%.

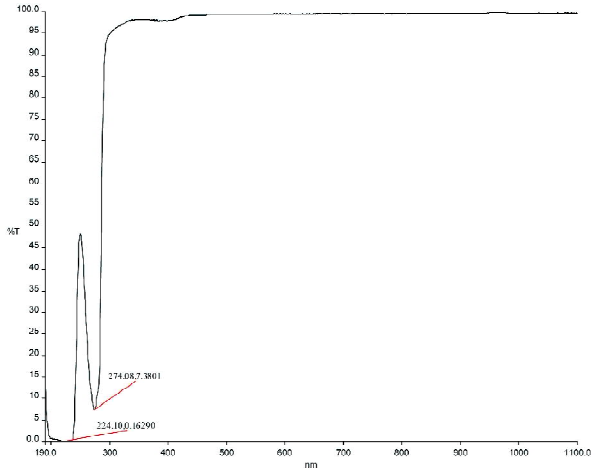


Fig.2 UV VIS-NIR Spectrum of grown crystal.

Thermal Analysis

Thermo gravimetric analysis (TGA) is a technique in which the weight of a substance is recorded as a function of temperature. In the present case, the TGA and DTA are carried out between 30° C and 93°C in the nitrogen atmosphere which provide an inert environment is shown in the Figure 3.

The TG curve provides with a quantitative measurement of mass change associated with the transition. It indicates that on melting the material decomposes and losses mass.

There are two weight losses of 31.66% and 58.02% noted in the thermo gram. Thus the curve shows a gradual mass loss. From the DTA curve, it was observed that there was a peak at 153 ^{0} C the melting point of the substance. Above this point, the material begins to attain an exothermic transition and begins to decompose

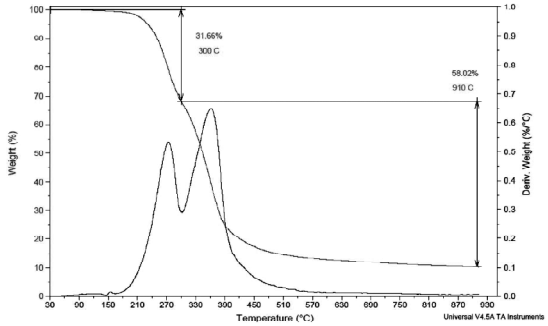
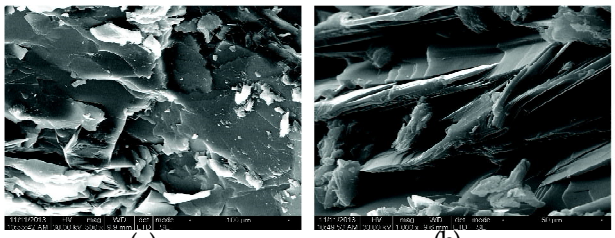


Fig.3 TGA-DTA Curves of grown crystal.

Scanning Electron Microscope Analysis

Scanning the surface with a high energy beam of electrons in a raster scan pattern is called Electron Microscope. The shape and size of the particles making up the object can be viewed and studied. Figures 4a and 4b show the SEM images of the grown up Atenolol crystal. The images show step-like growth which suggests the existence of grain boundaries and striations. The surface is smooth and free from any visible inclusions (Sachin and Nandre , 2013).



(a) (b)

Fig4 (a) SEM Micrograph of grown crystal
Fig4(b) Magnified SEM Micrograph of grown crystal

EDAX Analysis

Energy dispersive x-ray analysis (EDAX) is a micro analytical technique used to obtain information about the chemical composition of the grown up crystal. In this work, the grown up crystal was subjected to EDAX analysis. The EDAX spectrum of the pure Atenolol crystal is shown in the figure 5. The weight percentage (Wt %) of C, N and O as obtained from EDAX analysis is in concurrent with the theoretical valuesG

Element	Wt%	At%
CK	74.69	80.68
NK	08.52	07.89
OK	13.61	11.04
AuM	02.58	00.17
ClK	00.60	00.22
Matrix	Correction	ZAF

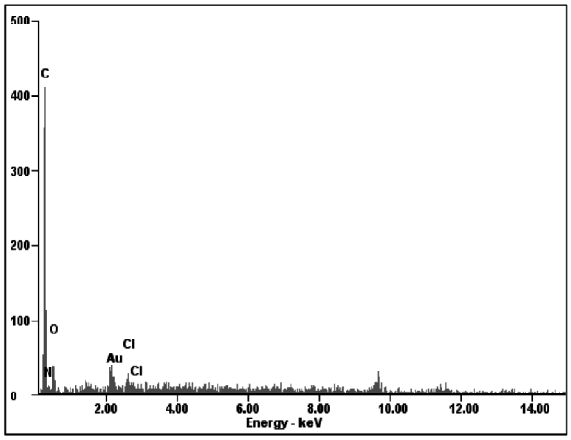


Fig.5 EDAX Spectrum of grown crystal

POWDER XRD Analysis

The grown up Atenolol crystals were finely powdered and subjected to powder XRD analysis. All the observed reflections were indexed. The sharp well defined Bragg's peaks were observed in the powder XRD pattern, which also show high crystalloid nature of Atenolol. The hkl values were indexed. The indexed powder XRD pattern of the growth of crystals is shown in the Figure 6.

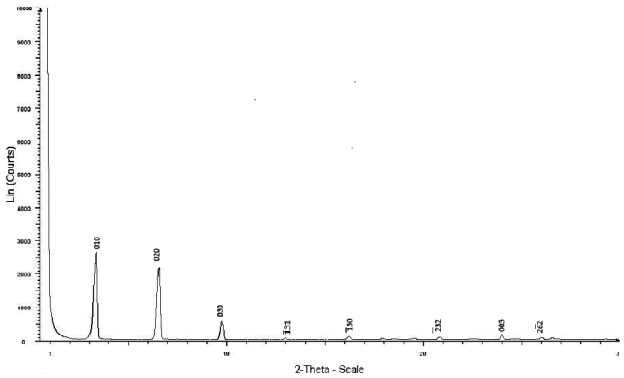


Fig.6 Indexed Powder XRD pattern of grown crystal

Optical Imaging Microscope

The sample is photographed using optical microscopy LX400. The photograph of the crystal is shown in the Figure 7

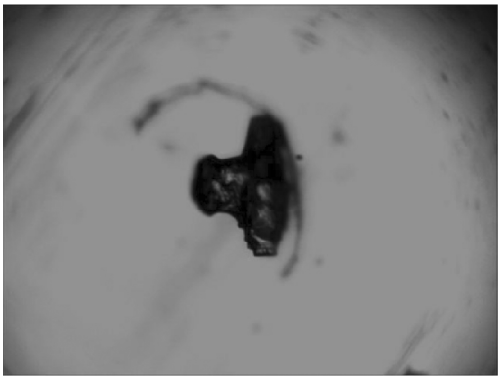


Fig.7 Optical image of grown crystal

CONCLUSION

Atenolol crystals were successfully grown by slow evaporation techniques. The FTIR studies confirmed the frequencies of vibrations of the molecule. From the thermo gram, it is concluded that these crystals are stable. The studies on optical transmission revealed that Atenolol crystals have low absorption in the entire visible region and the UV cut-off wavelength was found to be 224nm. The surface morphology of the crystal was understood by SEM studies. EDAX spectrum of the crystal confirms the stoichiometric composition of the elements. Powder XRD analysis reveals the quality and purity of the grown crystal.

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